UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,681	06/08/2001	Yihong Qiu	6437.US.P4	9430

23492 7590 06/23/2006

ROBERT DEBERARDINE
ABBOTT LABORATORIES
100 ABBOTT PARK ROAD
DEPT. 377/AP6A
ABBOTT PARK, IL 60064-6008

EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 06/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/877,681	QIU ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *9,11 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,12-15 and 17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8/20/01; 9/24/01; 10/01/01; 10/10/01; 12/03/01; 4/16/02.*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The receipt is acknowledged of applicants' IDS filed 08/20/2001, IDS filed 09/24/2001, IDS filed 10/01/2001, IDS filed 10/10/2001, IDS filed 12/03/2001, IDS filed 04/16/2002, and election filed 03/24/2003.

Response to Election/Restrictions

1. Applicant's election with traverse of Invention I, and species (b) for method of use, claims 1-8, 10, 12-15, and 17-21, in the reply filed on 03/24/2003 is acknowledged. The traversal is on the ground(s) that all the claims are related to valproate compounds such as valproate or divalproex sodium and formulation for their delivery with certain dissolution profiles. Both groups are classified in the same class and subclass and therefore have not given a separate status in the art. Searching both groups would not be burden on the examiner since the groups have the same classification. This is not found persuasive because valproate and divalproex sodium have different structure and different chemical properties, therefore can stand separate patents. Additionally, the prior art that anticipate group I may not anticipate group II. The search system and the focus of the invention are completely different, requiring an undue burden on the patent examiner. While searches may seem to be overlapping, however, extensive since the patent examiner searches the databases mostly literally. Rarely do applicants present claims to an inventions where the distinctness of the invention are readily clear such as

a chemical compound and a gene sequence. It is the responsibility of the examiner to enforce 35 USC 101, which allows the applicant to obtain a patent for a single invention. In the opinion of the examiner the applicants present two distinct inventions.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 9, 11, and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 03/24/2003.

Claims 1-8, 10, 12-15, and 17-21 are include din the prosecution.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-8, 10, 12-15, and 17-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for oral hydrophilic matrix formulation, does not reasonably provide enablement for any hydrophilic matrix formulation. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the breadth of the claims; the state of the prior art; the relative skill of those in the art; the amount of direction or guidance presented; the predictability or unpredictability of the art; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The nature of the invention: The nature of the invention hydrophilic matrix formulation suitable for once a day administration comprising divalproex sodium and polymer.

The breadth of the claims: The claims are broad. The claims encompass all kinds of formulations including transdermal and parentral formulations.

The state of the prior art: The state of the art does not recognize once a day transdermal or parentral formulations. The state of the art recognizes once a day oral administration of divalproex sodium, see US 4,913,906.

The relative skill of those in the art: The relative skill of those in the art is high.

The amount of direction or guidance presented: The specification provides no guidance, in the way written description, on any formulations other than oral formulation.

It is not obvious from the disclosure of oral formulation if the other formulations such as transdermal or parentral will work. *In re Dreshfield*, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result. A disclosure should contain representative examples which provide reasonable assurance to one skilled in the art that the formulations fall within the scope of a claim will possess the alleged activity. See *In re Riat et al.* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr et al.* (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

The predictability or unpredictability of the art: The lack of guidance from the specification and from the prior art with regard to formulation comprising divalproex sodium and hydrophilic polymer matrix administered transdermally or parentrally makes practicing the claimed invention unpredictable in the terms of administering the formulation by other routes such as transdermally or parentrally.

The presence or absence of working examples: The specification discloses only oral formulation, page 5, last paragraph and the examples. No working examples to show formulations other than oral formulation. Therefore, the specification has enabled only oral formulations.

The quantity of experimentation necessary: The art and the specification demonstrate oral formulation of divalproex sodium. Therefor, the practitioner would turn

to trial and error experimentation to practice the instant composition for delivering formulation other than oral to deliver divalproex sodium without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 20 depends on claim 22 that is not present.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,419,953. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the issued patent are directed to formulation comprising hydrophilic matrix comprising 50-55% of divalproex sodium and 20-40% of hydroxypropyl methyl cellulose. The difference between the present claims and the patented claims is that the patented claims do not recite the dissolution profile instantly claimed. However, it is expected that the formulation of the patent would have the same dissolution profile as the instant claims because both recite the same active ingredient and the hydrophilic polymer in the same amounts.

9. Claims 1-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,511,678. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the issued patent are directed to formulation comprising hydrophilic matrix comprising 40-80% of divalproex sodium and 20-40% of the same polymers having the same dissolution profiles.

10. Claims 1-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,528,090.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the issued patent are directed to formulation comprising hydrophilic matrix comprising 40-80% of divalproex sodium and 20-40% of the same polymers having the same pharmacokinetics and expected to have the same dissolution profile.

11. Claims 1-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,528,091. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the issued patent are directed to treating epilepsy using formulation comprising hydrophilic matrix comprising 50-55% of divalproex sodium and 20-40% of hydroxypropyl methyl cellulose. The difference between the present claims and the patented claims is that the patented claims do not recite the dissolution profile instantly claimed. However, it is expected that the formulation of the patent would have the same dissolution profile as the instant claims because both recite the same active ingredient and the same hydrophilic polymer in the amounts.

12. Claims 1-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,720,004. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the issued patent are directed

to formulation comprising hydrophilic matrix comprising 40-80% of divalproex sodium and 20-50% of the same polymers having the same dissolution profiles and pharmacokinetics.

13. Claims 1-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,713,086. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the issued patent are directed to formulation comprising hydrophilic matrix comprising 40-80% of divalproex sodium and 20-50% of the same polymers having the same pharmacokinetics and expected to have the same dissolution profile.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1-8, 10, 12-15, and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,913,906 (906).

US '906 teaches composition for controlled release of salts of valproic acid comprising 10-80% of the active agent and polymer additive such as methyl cellulose, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, and polyvinyl pyrrolidone, especially hydroxypropyl cellulose is preferred (abstract; col.2, lines 1-10, 63-68). The amount of the hydroxypropyl cellulose calculated to be up to 50% in the composition (col.2, lines 53-68; col.3, lines 1-3). The controlled release formulation results in sustained action of the drug with small fluctuation of the plasma level over prolonged period of time (col.1, lines 59-62). The composition is a once a day oral formulation that delivers the drug for 24 hour and shows about 97% dissolution rate profile after 24 hr. (col. 5 and 6, tables 1-4). Divalproex sodium is disclosed as one of the salts of valproic acid suitable for the formulation of the reference (col.5, lines 15-20). The reference disclosed that valproate used to treat epilepsy (col.1, line 44).

However, the reference does not explicitly teach the same dissolution profile as instantly claimed.

It is expected that the formulation of the prior art that comprises the same amount of the drug and the polymer to provide the same dissolution profile as instantly claimed. The prior art suggested divalproex sodium and also suggests the same polymers as instantly claimed.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to deliver once a day oral formulation comprising valproic acid salts and hydrophilic polymer as disclosed by US '906, and select the salt and the polymer that provide the sustained controlled release of the drug to provide dissolution profile according to specific patient need, motivated by the teaching of US '906 that controlled release formulation results in sustained action of the drug with small fluctuation of the plasma level over prolonged period of time, with reasonable expectation of having once a day formulation comprising divalproex sodium and hydrophilic polymer that provides sustained release of the drug with small fluctuation of the plasma level over prolonged period of time to provide dissolution profile that is best controls the patient epileptic condition.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Isis Ghali
Examiner
Art Unit 1615

IG

ISIS GHALI
PATENT EXAMINER